REMARKS

Amendments to the Claims

Claims 1, 8-12, 17-19, and 26-30 are pending. Claims 2-7, 13-15 and 20-25 have been previously withdrawn without prejudice as drawn to a non-elected invention. Claim 16 has been previously canceled without prejudice or disclaimer. Claim 29 has been canceled without prejudice with this amendment. Claims 1, 8, 11, 12, 17, 18 and 26 have been amended.

Claim 1 has been amended to clarify that the first assay system is capable of detecting the expression of SEQ ID NO: 5, to clarify that the test agent is identified as a candidate PTEN pathway modulating agent by determining a difference in the expression of SEQ ID NO: 5 in the presence or absence of the test agent, and to add steps (d) – (f), which recite the steps of (d) confirming that the test agent of (b) is a candidate PTEN pathway modulating agent by providing a second assay system comprising cultured cells or a non-human animal expressing SEQ ID NO: 5, wherein the second assay system measures a change in the PTEN pathway; (e) contacting the second assay system with the test agent of (b); and (f) determining a change in the PTEN pathway in the second assay system, wherein a change in the PTEN pathway between the presence and absence of said test agent confirms the test agent as a candidate PTEN pathway modulating agent.

Claim 8 has been amended to clarify that the SNF1LK nucleic acid is SEQ ID NO: 5.

Claim 11 has been amended to recite that the second assay system comprises cells defective in PTEN function and measures a phenotypic change that indicates that the PTEN pathway function is restored.

Claim 12 has been amended to clarify that the second assay system is a mouse model with defective PTEN function.

Claims 17 and 18 have been amended merely to correct their dependencies.

Claim 26 has been amended to delete reference to the phrases "a SNF1LK polypeptide encoded by a polynucleotide comprising SEQ ID NO: 5" and "a functionally active fragment encoded by a polynucleotide comprising SEQ ID NO: 5".

The claim amendments are made solely in an effort to advance prosecution and are made without prejudice, without intent to acquiesce in any rejection of record, and

without intent to abandon any previously claimed subject matter. Support for the claim amendments are found throughout the specification. No new matter has been added by way of these amendments.

Claim Objections

Claims 1 has been objected to because, according to the Office, it is not clear that SEQ ID NO: 5 is a polynucleotide sequence encoding SN1LK. Claim 1 has been amended to indicate that SEQ ID NO: 5 is a polynucleotide sequence that encodes SN1LK, thus obviating the objection. Applicant respectfully requests withdrawal of the objection to claim 1.

35 USC 102(b) Rejections

Claims 1, 8-9, 11-12, 17-19, and 26-29 were rejected under 35 USC 102(b) as being anticipated by US 2002/00257931 A1 (Meyers et al). Applicants respectfully traverse the rejections.

The Office stated that Meyers et al teach a polynucleotide that encodes at least a polypeptide comprising a functionally active fragment comprising amino acid residue 27-278 of the SNF1LK of SEQ ID NO: 5 (see SEQ ID NO: 1 in fig. 1) and also teach variants with 50%, 55%, 60%...98% identity to SEQ ID NO: 1 (which allegedly would encompass SEQ ID NO: 5 of the instant invention). The Office further stated that, in paragraphs [0029] and [0298] - [0301], Meyers et al teach a screening method for identifying modulators of the expression or activity of a protein encoded by SEQ ID NO: 1, including those having a stimulatory and inhibitory effect, comprising the steps of (1) providing an indicator composition comprising an activity of a SEQ ID NO: 1 encoded protein (this can be a fragment of SEQ ID NO: 1 with kinase activity), (2) providing a test compound, and (3) determining the effect of the test compound on activity.

With respect to disclosing a second assay system, the Office stated that Meyers et al further teach that toxicity and therapeutic efficacy of identified compounds can be determined by standard pharmaceutical procedures in cell cultures or experimental animals, e. g., for determining the LD50 (the dose lethal to 50% of the population) and the ED50 (the dose therapeutically effective in 50% of the population)

which is considered as a second assay in cells or non-human animals.

The Office concluded that the claims are anticipated by the teachings in Meyers et al., noting that the preamble of claim 1 was not given patentable weight, allegedly because the components and the steps in the method do not require additional components other than SNF1LK or a fragment thereof and an agent to be tested in vitro or in vivo.

Under 35 U.S.C. § 102(b), a claim is anticipated only if each and every element as set forth in the claim is found in a single art reference. *Verdegaal Bros. v. Union Oil Co.*, 814 F.2d 628, 631, 2 USPQ2d 1051, 10533 (Fed. Cir. 1987). No difference may exist between the claimed invention and the reference disclosure, as viewed by a person of ordinary skill in the field of invention. *In re Recombinant DNA Technology Patent and Contract Litigation*, 30 USPQ2d 1881 (S.D. Ind.1993). Further, the identical invention must be described or shown in as complete detail as is contained in the claim. *Richardson v. Suzuki Motor Co.*, 868 F.2d 1226, 1236 (Fed. Cir. 1989); *Chester v. Miller*, 15 USPQ2d 1333 (Fed. Cir. 1990); M.P.E.P. § 2131.

Moreover, to serve as an anticipatory reference, the prior art reference must provide an enabling disclosure of the claimed subject matter. *In re Hoeksema*, 399 F.2d 269 (CCPA 1968) ("In determining that quantum of prior art disclosure which is necessary to declare an applicant's invention' 'not novel' or 'anticipated' within section 102, the stated test is whether a reference contains an 'enabling disclosure'… ."). Thus, even if the claimed invention is disclosed in a printed publication, that disclosure will not suffice as prior art if it was not enabling. *Helifix Ltd. v. Blok-Lok, Ltd.*, 54 USPQ2d 1299 (Fed. Cir. 2000); *In re Donohoe*, 766 F.2d 531, 533 (Fed Cir. 1985); M.P.E.P. §2121.01. The mere naming or description of the subject matter is not considered an enabling disclosure if it cannot be produced without undue experimentation. *Elan Pharm., Inc. v. Mayo Found. For Med. Educ. & Research*, 346 F.3d 1051, 1054, 68 USPQ2d 1373, 1376 (Fed. Cir. 2003); *In re LeGrice*, 301 F.2d 929, 936 (CCPA 1962).

A reference is considered enabling if it describes the subject matter of the claimed invention sufficiently to have placed it in possession of the public. *Helifix Ltd. v. Blok-Lok, Ltd.*, 54 USPQ2d 1299 (Fed. Cir. 2000); *In re Donohue*, 766 F.2d 531, 533 (Fed. Cir. 1985); M.P.E.P. §2121.01. To place the invention in the possession of the public, the reference must be "so precise and so particular that any person skilled in the art to

which the invention belongs can construct and operate it without further experiments and without further exercise of inventive skill." *In re LeGrice*, 301 F.2d 929, 934 (CCPA 1962) (quoting I Robinson on Patents, Sec. 325 (1890)); *In re Brown*, 141 USPQ 245, (CCPA 1964).

The present invention is directed to methods of identifying a candidate PTEN pathway modulating agent. Using a *C. Elegans* genetic screen specifically designed to identify modifiers of the PTEN pathway, Applicants were the first ones to determine that SNF1LK is involved in the PTEN pathway. Based on this finding, the present claims are directed to a method of identifying a candidate PTEN pathway modulating agent using a first assay system capable of detecting the expression of a specified SNF1LK nucleic acid and a second assay system capable of measuring a change in the PTEN pathway.

Under 35 USC 102, to anticipate the claims as amended, Meyer et al must provide an enabling disclosure for a method of identifying a candidate PTEN pathway modulating agent comprising the steps of: (a) providing a first assay system comprising SEQ ID NO: 5 or a functionally active fragment thereof, wherein the assay system is capable of detecting the expression of SEQ ID NO: 5; (b) contacting the first assay system with a test agent that modulates SEQ ID NO: 5; (c) determining a difference in the expression of SEQ ID NO: 5 in the presence or absence of the test agent, wherein a difference in the expression of SEQ ID NO: 5 identifies the test agent as a candidate PTEN pathway modulating agent; (d) confirming that the test agent of (b) is a candidate PTEN pathway modulating agent by providing a second assay system that measures a change in the PTEN pathway; (e) contacting the second assay system with the test agent of (b); and (f) determining a change in the PTEN pathway in the second assay system, wherein a change in the PTEN pathway between the presence and absence of said test agent confirms the test agent as a candidate PTEN pathway modulating agent.

Initially, Applicants submit that the preamble of claim 1 should be given patentable weight. Whether to treat a preamble term as a claim limitation is "determined on the facts of each case in light of the claim as a whole and the invention described in the patent." *Storage Tech. Corp. v. Cisco Sys., Inc.*, 329 F.3d 823, 831 (Fed. Cir. 2003). The preamble is construed as a limitation of the claim "if it recites essential structure or steps, or if it is 'necessary to give life, meaning, and vitality' to the claim ." *Catalina Mktg. Int'l, Inc. v. Coolsavings.com, Inc.*, 289 F.3d 801, 808 (Fed. Cir. 2002), quoting

Pitney Bowes, Inc. v. Hewlett-Packard Co., 182 F.3d 1298, 1305 (Fed. Cir. 1999); *Kropa v. Robie*, 187 F.2d 150, 152 (CCPA 1951). In cases where the preamble sets forth the objective of the method and the body of the claim directs that the method be performed to obtain that objective, the courts have found that the preamble gives meaning to the claim. *Jansen v. Rexall Sundown Inc.,* 68 USPQ2d 1154 (Fed. Cir. 2003); *Rapoport v. Dement*, 254 F.3d 1053 (Fed. Cir. 2001). In addition, when the preamble recites additional structure or steps underscored as important by the specification, the preamble may operate as a claim limitation. *Corning Glass Works v. Sumitomo Elec. U.S.A., Inc.*, 868 F.2d 1251, 1257 (Fed. Cir. 1989).

In this case, the claims' recitation of a "method of identifying a candidate PTEN pathway modulating agent" gives life and meaning to the preambles' statement of purpose. The preamble is therefore not merely a statement of effect that may or may not be desired or appreciated. Rather, it is a statement of the intentional purpose for which the method must be performed. See *Jansen v. Rexall Sundown Inc.,* 68 USPQ2d 1154 (Fed. Cir. 2003). Accordingly, under current case law, the preamble is properly considered a limitation of the claim. Furthermore, contrary to the Office' contention, the components and the steps in the method do require components in addition to a SNF1LK nucleic acid or fragment thereof and an agent to be tested – i.e., steps (d) – (f) require a second assay comprising additional components able to measure a change in the PTEN pathway.

Applicants submit that Meyer et al. does not teach each and every step of the presently claimed methods and therefore fails to anticipate the instant invention. Meyer et al. teach certain polypeptide sequences having kinase activity and sequence homology to SNF1LK ("clone 3714"), polynucleotides encoding the polypeptides, and methods for modulating the expression or activity of the polypeptides. Meyer at al. makes no mention whatsoever of the PTEN pathway or any association between clone 3714 sequences and the PTEN pathway. Thus, Meyer et al. fails to even recognize that clone 3714 (i.e., SNF1LK) is involved in the PTEN pathway. Accordingly, Meyer et al. fails to teach a method for identifying a candidate PTEN pathway modulating agent using two separate assay systems that (1) detect the expression of SEQ ID NO: 5 and (2) measure a change in the PTEN pathway.

Furthermore, given that Meyers et al. does not contemplate identifying a

candidate PTEN pathway modulating agent , it fails to teach steps (d)- (f) of the claimed methods. Specifically, Meyer et al. fails to teach using a second separate assay system that measures a change in the PTEN pathway to confirm that the test agent is a candidate PTEN pathway modulating agent by contacting the second assay system with the test agent and determining a change in the PTEN pathway in the second assay system.

The Office argued that Meyer et al. teach using a second assay system to determine the toxicity and therapeutic efficacy of compounds identified as clone 3714 modulators. However, 35 USC 102 requires the prior art teaching to provide an enabling disclosure for each and every step of the claimed method. Furthermore, the identical invention must be described or shown in as complete detail as is contained in the claim. The teaching of the possible use of toxicity assays does not amount to a teaching of using a second assay system to measure a change in the PTEN pathway, much less amount to an enabling disclosure or a detailed description of such an assay system.

Given the failure of Meyer et al. to mention the PTEN pathway or recognize an association between SNF1LK and the PTEN pathway, it certainly fails to provide an enabling disclosure for the use of a first assay system to detect the expression of SEQ ID NO: 5 and a second assay system to measure a change in the PTEN pathway. More specifically, Meyer et al. fails to teach each and every step of claim 1 and therefore fails to anticipate the claimed methods. Accordingly, Applicant respectfully request withdrawal of the 35 USC 102 rejections.

35 USC 103(a) Rejections

Claim 10 was rejected under 35 USC 103(a) as allegedly being unpatentable over Meyers et al. in view of Summerton et al., (Biochimica et Biophysica Acta 1489: 141-158 (1999)) or Stein et al. (Antisense & Nucleic Acid Drug Dev., 7:151-157 (1997)). Applicants respectfully traverse the rejection.

The Office relied on the teachings of Meyer et al. as described above and stated that Summerton et al. and Stein et al. teach the advantages of using a PMO as an antisense oligomer. The Office alleged that it would have been obvious to use PMOs in the claimed methods to avoid the known problems associated with antisense technology and that one of

ordinary skill in the art would have had a reasonable expectation of success because the art teaches that RNase-dependent and RNase-independent oligos (ie PMOs) can be used interchangeably.

Contrary to the Office's allegations, the teachings of Meyer, Summerton and Stein, alone or in combination, do not render obvious the present invention. To meet the requirements for a *prima facie* case of obviousness, the Office must demonstrate that the references teach or suggest all the limitations of the claims. Post-KSR, the Board of Patent Appeals and Interferences (BPAI) has continued to maintain that:

> [A]n examiner must make "a searching comparison of the claimed invention — *including all its limitations* - with the teaching of the prior art." *In re Ochiai,* 71 F.3d 1565, 1572 (Fed. Cir. 1995) (emphasis added). Thus, "obviousness requires a suggestion of all limitations in a claim." *CFMT, Inc. v. Yieldup Intern. Corp.,* 349 F.3d, 1333, 1342 (Fed. Cir. 2003) (citing *In re Royka,* 490 F.2d 981, 985 (CCPA 1974)). *Ex Parte* Wada, BPAI, Appeal 2007-377, page 7 (Jan. 15, 2008) (unpublished). *See also, Ex parte* Shepard, BPAI, Appeal 2008-0401, page 7 (Jan. 3, 2008)(unpublished).

Applicants submit that Meyer, Summerton and Stein, alone or in combination, fail to teach or suggest a method for identifying a candidate PTEN modulating agent using a first assay system capable of detecting the expression of SEQ ID NO: 5 and a second assay system capable of measuring a change in the PTEN pathway.

First, for all of the reasons set forth above, Meyer et al. fails to teach or suggest all of the limitations of the claim. Specifically, Meyer et al. fails to teach steps (d)- (f) of the claimed methods. Further, neither Summerton nor Stein cure the deficiencies of Meyer et al. Neither Summerton nor Stein are concerned with SNF1LK or the PTEN pathway and therefore offer no teaching whatsoever in this regard. Thus, Summerton and Stein fail to supplement the teachings of Meyer et al. so as to arrive at the presently claimed methods of identifying a candidate PTEN modulating agent employing the steps of (a) – (f). Thus, the combined teachings of Meyer, Summerton, and Stein fail to teach or suggest <u>all of the limitations</u> of the presently claimed methods, and thus fail to render the instant invention obvious.

Furthermore, one skilled in the art would not have been motivated to modify the combined teachings of Meyer, Summerton and Stein to arrive at the presently claimed

methods. None of these references even mention the PTEN pathway. Thus, they fail to recognize any association between SNF1LK and the PTEN pathway and certainly fail to suggest with any reasonable expectation of success that an SNF1LK polynucleotide could be used in an assay to identify a PTEN pathway modulating agent.

Applicants respectfully submit that the Office has failed to establish a *prima facie* case of obviousness for the reasons set forth above. Accordingly, Applicant respectfully requests withdrawal of the 35 U.S.C. § 103(a) rejection based on the teachings of Meyer, Summerton and Stein.

Claim 10 was rejected under 35 USC 103(a) as allegedly being unpatentable over Meyers et al. in view of Martinez et al., (PNAS, 99: 14849-14854 (2002)). Applicants assume that the Office meant to reject claim 30 and not claim 10. Based on this assumption, Applicants respectfully traverse the rejection.

The Office applied the teachings described above to Meyer et al., acknowledging that Meyer et al. does not teach using an siRNA or dsRNA to modulate transcription. However, the Office relied on Martinez et al for teaching the use of siRNA to suppress the expression of mRNA targets. The Office alleged that it would have been obvious to design an siRNA to modulate the polynucleotide sequence of SEQ ID NO: 1 described in Meyer et al. (considered by the Office as a functional equivalent of SEQ ID NO: 5).

Meyer et al. fails to teach or suggest the claimed methods for the reasons previously discussed. Applicants submit that Martinez et al. fails to cure the deficiencies of the teachings of Meyer et al. Martinez et al. makes no mention of SNF1LK or the PTEN pathway and therefore offers no teaching whatsoever in this regard. Thus, Martinez et al. fails itself to supplement the teachings of Meyer et al. and also fails to provide a motivation to supplement the teachings of Meyer et al. so as to arrive at the presently claimed methods of indentifying a candidate PTEN pathway modulating agent. The combined teachings of Meyer et al. and Martinez et al. fail to teach or suggest all of the limitations of the presently claimed cells, and thus fail to render the instant invention obvious.

Applicants respectfully submit that the Office has failed to establish a *prima facie* case of obviousness for the reasons set forth above. Accordingly, Applicant respectfully

requests withdrawal of the 35 U.S.C. § 103(a) rejection based on the teachings of Meyer and Martinez et al.

Conclusion

In view of the foregoing amendments and remarks, the applicant submits that the claims are in condition for allowance, which is respectfully solicited. If the examiner believes a teleconference will advance prosecution, he is encouraged to contact the undersigned as indicated below.

Respectfully submitted,

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